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Abstract: This is the first comprehensive evaluation of completeness of case ascertainment in Swiss cancer registration. There is currently no method available that is considered to be the gold standard. Apart from simple measures such as the proportion of cases where registration was initiated by a death certificate and the proportion of diagnoses on the basis of histology or cytology/haematology, we applied two dedicated approaches: (i) the semiquantitative method of comparing the mortality to incidence rate ratio with relative survival (MI-Surv method) and (ii) the Flow method, which provides a quantitative estimate for the completeness depending on time since diagnosis. All 10 Swiss cancer registries in operation since at least 2006 and providing the required parameters were included. Simple and dedicated methods showed high completeness across all cancer registries and for most cancer types tested, with the notable exception of lymphoid leukaemia.

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Introduction

Population-based cancer registries (CRs) are an important source of data for health policies, surveillance and epidemiological research. Cancer incidence or survival measures derived from such data depend on the completeness of case ascertainment, that is the extent to which all diagnosed neoplasms in the resident population are included in the registry database.

Several methods for assessing the completeness of registration have been devised and evaluated (Bullard *et al.*, 2000; Silcocks and Robinson, 2007; Schmidtmann, 2008; Parkin and Bray, 2009). Semiquantitative methods assess completeness indirectly without quantifying the number of missing cases. These include historic data methods checking the stability of incidence rates over time or comparing them with standard values, given that such standards are available (Curado *et al.*, 2007; Hackl *et al.*, 2011). The average number of notifications per case is often reported, which is expected to be correlated with completeness, whereas an unusually high proportion of diagnoses on the basis of histology or cytology/haematology (MV%) might indicate over-reliance on pathology laboratories as sources of information, thus indicating potential under-registration (Bray and Parkin, 2009). Another indirect measure of completeness is the proportion of cases where registration was initiated by a death certificate (DCN%). If CRs rely on death certificates to a large extent, a number of missed diagnoses are to be expected because of the well-documented inaccuracy and lack of specificity of the certified causes of death (Mathers *et al.*, 2005). Furthermore, the probability for a cancer diagnosis to appear on the death certificate decreases with time after diagnosis (Bullard *et al.*, 2000). Completeness of cancer registration can also be assessed by comparing the mortality/incidence ratios (MI ratios) with reference registries considered to be complete and to share the same expected ratios (Haberland *et al.*, 2001; Hofferkamp, 2008). Reference MI ratios are not required if the MI ratio is compared with relative survival (RS) estimates from the same CR because both are expressions of the same case fatality rate (MI-Surv method) (Parkin and Bray, 2009; Vostakolaei *et al.*, 2010).

Quantitative methods aim to directly estimate the number of missed diagnoses. Traditionally, they comprise variations of the capture–recapture design, where the registry database is compared with another collection of cancer diagnoses, for example data collected for clinical or epidemiological studies or administrative datasets such as the national vital statistics. A novel and simpler

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method was introduced by Bullard *et al.*, 2000. This so-called Flow method models the logical flow of data in the registration system. The Flow method has been validated using simulated data (Silcocks and Robinson, 2007) and is currently the standard practice in the UK (NHS Cancer Plan, 2004). The EUROCOURSE Workpackage on completeness and timeliness of cancer registration data in Europe specifically encourages a wider dissemination of the Flow method (Zanetti *et al.*, 2010).

A survey on the different completeness methods used by European CRs was conducted recently (Zanetti *et al.*, 2015). Only half of the responding registries declared the use of at least one quantitative method and only one in five stated that they had published the results in a peer-reviewed journal. Hence, there seems to be a reporting deficit on the levels of completeness in many European CRs despite the importance of completeness for unbiased statistics.

Methods

Source of cancer incidence data

This study is based on the National Core Dataset managed by the National Institute for Cancer Epidemiology and Registration with the purpose of national cancer monitoring in Switzerland. All 10 Swiss CRs in operation since at least 2006 are included in this report: Basel (BA), Fribourg (FR), Geneva (GE), Grison and Glarus (GG), Neuchâtel and Jura (NJ), St. Gallen-Appenzell (SG), Ticino (TI), Valais (VS), Vaud (VD) and Zurich (ZH). Included are malignant primary cancer cases. Vital status was followed up until at least 2012. The diagnosis period 2006 to 2011 was pooled, except for BA, where 2006–2009 was available at the time of analysis. All cancer diagnoses (excluding nonmelanotic skin cancer) amounted to 9350 (BA), 7270 (FR), 13 520 (GE), 7250 (GG), 7580 (NJ), 14 520 (SG), 11 520 (TI), 9420 (VS), 20 610 (VD) and 36 530 (ZH).

Source of cancer-specific mortality data

Registration of death is mandatory. The Swiss cause of death statistics is comprehensive and based on data from civil registries and death certificates issued by doctors (Roy and Junker, 2014). The coding is based on the 10th revision of the International Classification of Diseases coding system (ICD-10) and is conducted by the Federal Statistical Office according to rules defined by the WHO since 1995. Deaths from 2006 to 2011 were pooled (in BA: 2006–2009) for cancer-specific mortality rates.

Source of population data

Permanent residential population at mid-year was provided by the Federal Statistical Office. The permanent resident population comprises all Swiss citizens with main place of residence in Switzerland, and foreign citizens with a residence permit for at least 12 months.

MI-Surv method

The crude ratio of mortality to incidence rates (MI ratio) and the crude complement of relative survival (1 – RS) were derived for identical periods of time and regional populations at risk. The statistical test comparing MI ratios of individual CRs with the nationally pooled MI ratio was performed according to Parkin and Bray (2009). RS estimation excluded cases with a death certificate as the only source of information (DCO) (2.3%). Patients with multiple primary tumours were included. Cases without active follow-up were excluded (1.7%). RS was calculated as the ratio of the observed survival of cancer cases and the expected survival of individuals in the general population matching in age, sex and calendar year of death (Ederer *et al.*, 1961). Expected cancer survival was estimated using the Ederer II method applied to all-cause mortality tables (Ederer *et al.*, 1959). RS was estimated using the strs command (version 1.4.2) written by Dickman and Coviello (2015). The period survival approach (Brenner and Gefeller, 1996) was applied with follow-up dates 2006–2012. Five-year RS was used for the MI-Surv method for all types of cancer, except breast and prostate cancer, where, to comply with the assumption of negligible excess hazard inherent to the MI-Surv method, the 10-year RS was considered more adequate (Dehler *et al.*, 2013; Bouchardy *et al.*, 2015). VD was not analysed with the MI-Surv method because information on survival was unavailable at the time of analysis.

Flow method

Completeness of case ascertainment was modelled as described in Bullard *et al.* (2000). The Flow method estimates three processes depending on time t after diagnosis: survival times $s(t)$, intervals from diagnosis until registration during the patient lifetime $u(t)$ and proportions of death certificates that retain a mentioning of cancer $m(t)$. Patients not yet captured by registration are either 'still missing' but alive or 'lost' because they have died, have not been registered during life and their death certificate lacked a mention of cancer. The estimated completeness is the proportion neither 'still missing' nor 'lost'. The variance and confidence interval for completeness and lost proportions were derived with the direct bootstrap method (1000 samples). For individuals with multiple primary diagnoses, only the first diagnosis was accepted to comply with the assumption of independent cases. Cumulative observed survival $s(t)$ was estimated on the basis of diagnoses 2006–2011 for all CRs. The probability of failure of registration before death $u(t)$ was estimated on the basis of registered patients who died 2007–2012, except for FR, where deaths 2006–2012 were used, because of the small number of cases. A lower limit of 50 cases was required for $u(t)$ estimation, which excluded Hodgkin lymphoma. Time intervals from diagnosis to registration were censured to 1 year before the date of death if death occurred before registration because the registration probability

Table 1 **Simple routine measures of completeness**

	ZH[a]		FR[b]		TI		VS		GE		BA[c]		SG		GG		NJ		VD		All CRs	
Cancer types	DCN%	MV%	DCN%	MV%	DCN%	MV%	DCN%	MV%	DCN%	MV%	DCN%	MV%	DCN%	MV%	DCN%	MV%	DCN%	MV%	DCN%	MV%	DCN%	MV%
Lip, oral cavity and pharynx	1.5	98.7	1.0	98.6	0.0	99.4	0.9	98.5	1.2	98.0	0.0	99.2	1.0	98.5	1.3	97.5	–	98.0	–	99.1	1.0	98.7
Oesophagus	6.8	96.1	0.0	100	0.0	98.7	1.9	94.9	0.5	95.9	3.0	98.7	2.8	98.9	3.1	98.0	–	92.4	–	96.1	2.9	96.7
Stomach	5.7	95.8	0.0	98.9	2.0	98.0	1.7	96.2	1.7	98.3	2.6	97.8	3.5	96.5	2.3	97.2	–	99.3	–	97.2	2.9	97.1
Colon, rectum and anus	3.4	97.1	2.3	97.3	1.2	98.1	1.1	96.6	1.8	96.7	1.6	98.6	1.7	98.1	2.6	96.2	–	96.4	–	97.7	2.1	97.4
Liver	**10.5**	60.1	2.5	66.7	6.1	38.0	4.9	43.7	8.8	45.6	**10.7**	**94.4**	9.6	69.0	7.3	55.0	–	59.1	–	59.4	7.8	56.7
Pancreas	**13.5**	75.1	8.2	77.6	**11.0**	65.1	3.8	66.2	**10.8**	77.1	**17.1**	86.4	**11.3**	78.8	**10.6**	78.9	–	66.5	–	66.1	**11.1**	73.7
Lung (including trachea)	6.7	91.0	3.6	94.6	3.0	91.0	1.6	91.4	4.8	90.2	2.1	95.9	4.6	91.9	3.6	91.7	–	91.6	–	91.9	4.2	91.9
Melanoma of the skin	0.3	99.7	0.0	100	0.2	99.8	0.0	100	0.0	99.9	0.5	96.4	0.1	99.9	0.0	100	–	100	–	99.8	0.2	99.6
Breast (female)	1.3	98.6	0.0	99.3	0.3	99.2	0.3	98.4	0.6	98.7	0.8	99.4	1.0	98.5	1.0	98.8	–	99.4	–	98.5	0.8	98.8
Cervix and corpus uteri	2.3	98.2	1.2	97.8	1.2	98.5	0.8	99.6	0.3	99.5	0.6	99.3	2.6	97.0	1.0	98.5	–	98.2	–	98.1	1.5	98.4
Ovary	5.2	93.1	1.7	100	1.1	98.9	1.2	95.3	3.0	94.1	0.0	96.4	1.9	95.9	7.1	90.3	–	94.0	–	95.3	2.9	95.0
Prostate	2.6	94.0	0.4	98.0	2.4	91.9	1.3	93.7	1.9	94.7	1.7	98.1	1.5	96.3	1.5	94.9	–	92.2	–	96.3	1.8	95.1
Kidney	5.8	86.9	4.1	90.7	1.0	91.4	1.3	88.8	4.0	92.0	1.9	95.8	2.7	86.9	0.6	89.7	–	91.9	–	94.5	3.1	90.4
Bladder	4.0	94.9	0.8	97.0	1.7	96.9	1.0	94.9	1.5	97.8	0.6	98.7	2.9	96.8	0.7	97.1	–	97.8	–	97.2	2.1	96.6
Eye, brain and CNS	7.2	85.1	1.2	82.2	5.4	84.5	1.3	77.8	5.9	86.0	2.6	92.1	5.9	81.6	2.3	77.1	–	85.3	–	89.0	5.0	84.8
Hodgkin lymphoma	0.7	99.6	0.0	100	0.0	100	0.0	100	0.0	100	0.0	98	0.0	100	0.0	100	–	100	–	100	0.2	100
Non-Hodgkin lymphoma	2.2	98.5	2.9	99.2	1.2	99.2	0.0	99.7	0.9	99.8	1.9	97.4	2.2	96.4	1.2	98.1	–	100	–	98.2	1.6	98.5
Multiple myeloma	4.7	93.9	0.0	98.9	6.0	88.7	0.8	95.9	3.2	86.4	3.6	94.7	2.8	100	6.5	100	–	99.1	–	94.9	3.9	94.7
Lymphoid leukaemia	8.3	95.6	0.0	100	3.1	98.1	2.1	99.3	2.5	99.6	3.1	92.0	4.9	100	3.3	100	–	100	–	93.3	4.3	97.2
Myeloid leukaemia	4.4	98.0	0.0	100	2.7	99.1	2.3	98.9	6.9	99.4	0.0	95.1	4.0	100	4.3	100	–	100	–	96.2	3.9	98.3
All sites[d]	3.9	94.2	1.6	96.2	2.3	92.4	1.4	92.7	2.7	94.0	2.4	95.7	3.0	94.8	2.6	94.2	–	93.6	–	94.4	2.7	94.2

DCN% $\geq$ 10 and significantly large MV% ($P < 0.05$) are in bold.

BA, Basel; CNS, central nervous system; DCN%, proportion of diagnoses 2006–2011 by cancer type and cancer registry where the death certificate was the first notification; FR, Fribourg; GE, Geneva; GG, Grison and Glarus; MV%, proportion of diagnoses with microscopic verification; NJ, Neuchâtel and Jura; SG, St. Gallen-Appenzell; TI, Ticino; VD, Vaud; VS, Valais; ZH, Zurich.

[a]DCN 2009–2011.

[b]DCN 2009, 2011, 2012.

[c]DCN 2006–2007.

[d]Except nonmelanotic skin cancer.

Table 2 Difference in crude mortality-incidence ratios from the complement of crude relative survival proportions

	ZH			FR			TI			VS			GE			BA			SG			GG			NJ			All CRs		
Cancer types	ΔMI-Surv (%)	LB (%)	UB (%)	ΔMI-Surv (%)	LB (%)	UB (%)	ΔMI-Surv (%)	LB (%)	UB (%)	ΔMI-Surv (%)	LB (%)	UB (%)	Δ MI-Surv (%)	LB (%)	UB (%)	ΔMI-Surv (%)	LB (%)	UB (%)	ΔMI-Surv (%)	LB (%)	UB (%)	ΔMI-Surv (%)	LB (%)	UB (%)	ΔMI-Surv (%)	LB (%)	UB (%)	ΔMI-Surv (%)	LB (%)	UB (%)
Lip, oral cavity and pharynx	−9.8	−14.9	−4.8	−7.7	−21.6	6.2	−9.0	−19.3	1.3	−11.0	−21.4	−0.5	−9.0	−17.0	−0.9	−3.2	−14.8	8.4	−2.2	−11.0	6.6	−6.6	−20.1	6.8	−5.6	−19.1	7.9	−6.4	−9.5	−3.3
Oesophagus	−1.3	−12.5	10.0	4.0	−19.2	27.2	−11.9	−30.1	6.3	−2.3	−22.2	17.7	3.0	−15.2	21.1	27.8	−0.5	56.1	−1.0	−19.1	17.2	−8.2	−32.7	16.3	12.7	−15.3	40.8	1.7	−4.7	8.0
Stomach	−9.7	−17.9	−1.6	−3.6	−22.2	15.1	−4.6	−16.0	6.9	−13.4	−27.4	0.6	−13.2	−25.6	−0.9	−5.3	−21.4	10.8	−8.4	−20.5	3.7	3.9	−14.2	22.1	−11.9	−30.1	6.2	−8.3	−12.7	−4.0
Colon, rectum and anus	1.6	−1.2	4.5	1.5	−5.6	8.6	−0.8	−5.5	3.9	0.1	−6.0	6.1	−1.7	−6.1	2.7	1.5	−3.7	6.7	1.5	−3.0	5.9	1.6	−5.1	8.4	0.0	−6.1	6.1	1.0	−0.6	2.6
Liver	0.8	−9.8	11.4	17.0	−10.7	44.7	−8.6	−20.3	3.2	−14.4	−28.9	0.1	−4.4	−18.6	9.7	**62.2**	**24.7**	**99.6**	−10.2	−25.9	5.4	−3.3	−26.6	20.0	12.3	−10.5	35.2	0.2	−5.2	5.6
Pancreas	−0.1	−8.1	7.9	1.6	−17.3	20.6	−4.1	−17.4	9.2	4.9	−12.4	22.3	−11.4	−23.4	0.5	**54.3**	**29.7**	**78.8**	−4.8	−16.7	7.2	−11.0	−28.5	6.6	−2.7	−20.5	15.1	0.7	−3.9	5.2
Lung (including trachea)	−6.4	−10.3	−2.5	4.6	−5.0	14.2	−5.5	−12.1	1.1	−11.8	−18.9	−4.6	−8.5	−14.8	−2.3	4.5	−3.9	12.8	−9.2	−15.4	−3.0	−7.2	−16.2	1.8	−9.4	−17.4	−1.4	−5.7	−7.9	−3.5
Melanoma of the skin	2.8	0.4	5.1	0.6	−5.3	6.5	2.5	−2.3	7.3	−1.6	−7.3	4.1	2.9	−0.4	6.2	5.5	−0.5	11.6	1.4	−2.7	5.5	3.4	−3.0	9.9	5.3	0.2	10.5	2.3	0.9	3.7
Breast (female)	−6.3	−9.2	−3.4	ND	–	–	1.8	−2.2	5.9	−6.8	−11.4	−2.2	1.3	−1.8	4.4	−1.8	−6.9	3.4	2.5	−1.4	6.4	3.0	−2.8	8.8	−1.0	−6.2	4.2	−1.2	−2.6	0.1
Cervix and corpus uteri	4.2	−0.3	8.7	2.4	−9.3	14.2	5.9	−1.6	13.5	−1.7	−11.0	7.6	−2.2	−9.6	5.2	−0.4	−8.7	8.0	2.8	−4.1	9.8	−3.3	−13.9	7.3	−2.7	−13.2	7.9	2.0	−0.6	4.6
Ovary	**13.1**	**2.7**	**23.6**	19.7	−1.8	41.3	13.1	−4.0	30.1	−1.5	−18.5	15.4	3.7	−10.7	18.1	**42.2**	**18.0**	**66.3**	4.8	−9.6	19.2	18.9	−5.2	42.9	13.3	−8.1	34.6	**12.3**	**6.7**	**17.8**
Prostate	−5.9	−9.1	−2.6	ND	–	–	0.9	−4.2	6.1	−9.8	−15.5	−4.0	3.5	−0.6	7.6	−6.7	−11.6	−1.9	3.3	−0.6	7.2	−8.9	−15.1	−2.7	0.8	−5.7	7.3	−1.9	−3.5	−0.3
Kidney	2.7	−3.5	8.9	6.1	−11.1	23.2	6.1	−3.7	15.9	−5.2	−17.0	6.7	−1.4	−10.7	7.8	11.7	−1.0	24.5	2.1	−7.3	11.5	−0.3	−14.6	14.0	0.1	−14.3	14.5	3.0	−0.4	6.5
Bladder	1.1	−5.1	7.3	9.6	−6.4	25.6	−2.5	−11.9	6.8	−7.6	−19.0	3.8	−1.1	−10.9	8.6	−6.0	−17.3	5.3	4.5	−6.2	15.3	−4.4	−15.7	6.8	−6.9	−17.8	4.0	−1.6	−4.9	1.7
Eye, brain and CNS	−2.3	−11.0	6.4	−7.9	−30.3	14.4	−1.8	−20.2	16.7	2.3	−17.1	21.7	−8.3	−23.8	7.3	10.3	−11.5	32.1	3.7	−10.6	18.0	−9.8	−28.4	8.8	7.6	−18.6	33.8	−0.7	−6.0	4.6
Hodgkin lymphoma	0.7	−5.2	6.6	**12.2**	**2.4**	**22.0**	−4.7	−17.3	8.0	−1.2	−17.3	14.8	−4.5	−14.3	5.3	0.2	−17.4	17.7	−4.1	−14.3	6.2	−4.8	−19.9	10.2	10.2	−8.1	28.5	−0.6	−4.3	3.2
Non-Hodgkin lymphoma	4.1	−0.2	8.4	6.2	−4.9	17.3	9.7	1.7	17.8	6.9	−2.3	16.0	0.0	−6.6	6.6	1.1	−7.5	9.6	3.4	−3.9	10.6	0.7	−11.0	12.3	7.9	−3.1	18.8	4.1	1.5	6.6
Multiple myeloma	4.5	−4.8	13.8	6.8	−19.3	32.9	4.0	−12.6	20.6	0.8	−18.8	20.4	10.1	−9.0	29.1	25.0	−0.5	50.4	0.8	−13.8	15.4	0.0	−21.0	21.0	7.0	−16.2	30.2	6.3	0.7	12.0
Lymphoid leukaemia	**13.8**	**6.1**	**21.5**	16.9	−0.4	34.2	2.7	−7.8	13.3	**13.6**	**0.3**	**27.0**	2.6	−8.0	13.2	**31.6**	**11.6**	**51.5**	**20.2**	**7.0**	**33.4**	**20.1**	**4.6**	**35.7**	**20.5**	**0.9**	**40.1**	**14.0**	**9.8**	**18.3**
Myeloid leukaemia	0.3	−10.9	11.4	5.7	−22.6	34.0	12.0	−12.3	36.3	6.2	−19.9	32.3	4.1	−14.2	22.5	14.2	−9.5	38.0	1.4	−16.1	18.9	3.6	−19.6	26.9	−7.8	−35.2	19.6	4.2	−2.3	10.8
All sites[a]	5.9	4.9	6.9	6.4	4.1	8.8	4.7	2.9	6.5	−0.2	−2.1	1.8	3.5	2.0	5.0	**11.0**	**9.0**	**13.1**	4.6	3.0	6.2	3.8	1.6	6.0	4.0	1.7	6.3	5.4	4.8	5.9

Differences above +10% with confidence interval excluding zero are in bold.

BA, Basel; CNS, central nervous system; FR, Fribourg; GE, Geneva; GG, Grison and Glarus; LB, lower limit of the 95% confidence interval; ΔMI-Surv, difference between crude mortality–incidence ratios and the complement of crude relative survival proportions; ND not determined; NJ, Neuchâtel and Jura; SG, St. Gallen-Appenzell; TI, Ticino; UB, upper limit of the 95% confidence interval; VS, Valais; ZH, Zurich.

[a]Except nonmelanotic skin cancer.

Table 3 Flow method-estimated completeness of case ascertainment three years after diagnosis for diagnoses 2006 to 2011

	ZH			FR			TI			VS			GE			SG			GG			All CRs		
Cancer types	Completeness (%)	LB (%)	UB (%)	Completeness (%)	LB (%)	UB (%)	Completeness (%)	LB (%)	UB (%)	Completeness (%)	LB (%)	UB (%)	Completeness (%)	LB (%)	UB (%)	Completeness (%)	LB (%)	UB (%)	Completeness (%)	LB (%)	UB (%)	Completeness (%)	LB (%)	UB (%)
Lip, oral cavity and pharynx	93.7	91.4	95.8	96.6	88.4	99.9	98.8	96.6	99.8	98.2	95.2	99.8	98.8	98.3	99.1	97.1	94.1	99.6	97.8	89.6	99.6	96.3	95.4	97.2
Oesophagus	97.9	95.7	99.5	98.8	87.3	99.4	99.7	96.1	99.8	99.8	98.2	99.9	97.5	94.5	98.5	95.0	89.2	99.4	99.7	96.9	99.8	97.8	96.5	98.8
Stomach	95.7	94.2	97.2	95.4	90.0	100.0	96.3	93.0	99.4	98.6	94.9	99.5	95.6	91.8	99.1	97.8	95.0	99.6	96.8	92.2	99.7	95.9	94.8	96.9
Colon, rectum and anus	93.4	92.4	94.2	97.2	93.8	100.0	97.8	96.6	98.9	97.5	95.4	99.1	97.6	96.3	98.6	96.7	95.3	97.9	96.6	94.8	98.4	95.8	95.3	96.2
Liver	89.2	86.3	91.4	100.0	94.4	100.0	91.6	88.1	94.7	95.6	93.7	96.6	88.1	84.3	92.0	88.4	85.3	91.3	93.2	81.6	96.4	89.8	88.5	91.2
Pancreas	97.4	97.0	97.5	94.3	91.0	97.3	95.9	94.0	97.5	98.2	95.4	99.7	94.0	92.0	95.9	97.9	96.2	99.0	94.4	90.1	98.7	96.3	95.5	96.9
Lung (including trachea)	94.4	93.7	95.1	97.4	93.9	99.9	96.8	95.4	98.6	96.3	94.9	97.8	93.0	91.7	94.4	96.9	95.7	97.9	94.6	92.6	97.4	95.3	94.8	95.7
Melanoma of the skin	91.4	88.9	93.9	93.9	85.3	100.0	87.6	81.1	92.7	98.3	94.9	99.8	99.0	97.4	99.7	97.2	95.1	99.1	95.8	90.6	99.5	93.6	92.2	94.9
Breast (female)	90.9	89.7	91.9	98.5	93.0	100.0	96.0	94.3	97.6	98.4	96.9	99.8	97.0	95.5	98.1	97.8	96.5	98.9	95.9	93.7	97.9	94.8	94.1	95.3
Cervix and corpus uteri	90.4	87.3	93.0	94.9	79.3	100.0	99.2	97.3	100.0	99.9	98.8	100.0	99.6	97.7	99.7	93.2	89.7	96.4	98.7	90.6	99.5	94.8	93.4	96.1
Ovary	97.0	95.0	98.8	95.7	82.7	100.0	97.8	95.1	100.0	97.5	94.0	99.9	94.7	90.6	97.8	96.4	92.9	99.4	96.5	89.6	98.8	96.3	95.0	97.4
Prostate	**82.2**	**80.8**	**83.6**	93.4	87.3	99.3	87.3	83.8	90.6	**86.6**	**83.6**	**89.4**	89.6	87.2	92.1	94.5	93.1	95.7	92.2	89.8	94.7	**87.9**	**87.2**	**88.7**
Kidney	**83.9**	**79.6**	**87.5**	100.0	85.0	100.0	99.6	96.8	99.8	93.2	86.8	98.8	91.3	81.7	96.8	89.6	83.1	95.4	95.4	90.4	99.2	89.7	87.6	91.5
Bladder	91.4	89.4	93.1	99.1	84.9	99.5	96.6	94.1	98.6	95.1	91.8	97.7	97.3	96.5	97.9	97.2	95.3	99.0	99.3	97.9	99.6	93.9	92.8	94.8
Eye, brain and CNS	93.4	91.1	95.4	95.6	86.8	98.9	98.8	88.6	99.1	91.8	86.2	95.9	92.0	87.3	95.7	95.8	92.6	98.6	84.6	76.0	94.8	92.7	91.2	94.1
Non-Hodgkin lymphoma	**87.7**	**85.5**	**89.9**	99.4	87.0	99.6	94.4	91.2	97.1	98.4	95.4	99.7	95.1	92.6	97.4	95.5	92.0	99.1	98.6	97.7	99.1	92.1	90.8	93.3
Multiple myeloma	91.4	89.0	93.5	97.2	89.1	100.0	94.4	89.9	98.1	92.6	86.9	96.8	85.0	77.3	92.2	97.5	93.7	99.3	90.3	82.6	100.0	91.3	89.7	92.9
Lymphoid leukaemia	**71.9**	**66.4**	**77.1**	88.0	59.6	99.6	**71.4**	**57.7**	**86.6**	**67.3**	**57.2**	**77.0**	**75.9**	**67.8**	**83.3**	**80.3**	**73.6**	**86.6**	**79.0**	**66.6**	**100.0**	**73.1**	**70.1**	**76.2**
Myeloid leukaemia	97.7	93.7	99.7	100.0	82.2	100.0	88.1	79.6	95.4	96.0	88.6	99.4	87.8	81.7	93.0	81.9	72.5	96.3	85.4	69.6	99.7	89.8	87.0	92.6
All sites[a]	89.6	89.2	90.0	93.7	91.5	95.8	93.0	92.2	93.9	92.8	91.8	93.6	93.0	92.3	93.6	94.4	93.8	95.0	92.3	91.1	93.5	92.1	91.8	92.3

Completeness estimates <80% or 80–89% with confidence intervals <90% are in bold.

CR, cancer registy; CNS, central nervous system; FR, Fribourg; GE, Geneva; GG, Grison and Glarus; LB, lower limit of the 95% confidence interval; SG, St. Gallen-Appenzell; TI, Ticino; UB, upper limit of the 95% confidence interval; VS, Valais; ZH, Zurich.

[a]Except nonmelanotic skin cancer.

increased by 15–20% during the year before death (Lorez M, unpublished data) and $u(t)$ should be applicable to all cases alive (Bullard *et al.*, 2000). Estimation of $m(t)$ was based on time periods with less than 5% missing information on cause of death. These were 2007–2011 for TI, GE, SG, GG and period 2005 to 2009 for VS. In FR (2006–2012) and ZH (2009–2012), up to 40% of deaths were without information on causes; thus, estimation of $m(t)$ may be biased. Function $m(t)$ was estimated by logistic regression. BA, VD and NJ were not analysed using the Flow method because of lack of information on causes of death.

Results

For all 10 Swiss CRs in operation since at least 2006, the DCN% was only 2.7% for all cancer sites combined (Table 1). Systematically high DCN% were found for hepatic and pancreatic cancer, up to 10.7 and 17.1%, depending on CR.

The MV% was 94.2% overall (Table 1). CR-specific MV % were tested by cancer type for being significantly greater than the pool of all 10 Swiss CRs (Bray and Parkin, 2009). As a result, only hepatic cancer in BA was flagged (MV = 94.4%).

The ratios of crude mortality and incidence rates (MI ratio), by cancer type and CR, were compared with the pooled MI ratios (Supplementary Table S1, Supplemental digital content 1, *http://links.lww.com/EJCP/A166*). Significantly high MI ratios (expressed as %) were found in BA for cancers of liver (146%), pancreas (139%), oesophagus (112%), ovary (92%), multiple myeloma (86%), melanoma (19%) and all sites combined (49%), and isolated findings in FR for kidney cancer (51%) and in NJ for Hodgkin lymphoma (22%).

Differences between MI ratio and 1 − RS (ΔMI-Surv) by cancer type and CR are listed in Table 2. Significant ΔMI-Surv values greater than +10% are flagged as potentially under-registered. Flagging showed two patterns. First, lymphoid leukaemia was systematically marked in a majority of CRs and in all CRs combined (14.0%). Second, BA was repeatedly flagged: for hepatic (62.2%), pancreatic (54.3%) and ovarian cancer (42.2%), and for all sites combined (11.0%). Isolated flags occurred for ovarian cancer in ZH (13.1%) and Hodgkin lymphoma in FR (12.2%).

Flow method-estimated levels of completeness at 3 years after diagnosis are listed in Table 3. Completeness was flagged if the point estimate was less than 80% or if the confidence interval excluded 90%. Each CR tested reached the international level for satisfactory completeness of 90% ~3 years after the diagnosis for all sites combined, as well as for the majority of cancer types. The only diagnostic group that seemed systematically under-registered was again lymphoid leukaemia, which was flagged in six of seven registries. CR-specific findings were lower levels of completeness in ZH for prostate cancer, kidney cancer and non-Hodgkin lymphoma, and prostate cancer in VS. The yearly increase in completeness, as well as in cases lost from registration, is shown in Supplementary Table S2 (Supplemental digital content 2, *http://links.lww.com/EJCP/A167*) for all cancer types combined. A majority of CRs reached completeness levels of 90% already 2 years after diagnosis. In addition to high completeness, the proportions of cases expected to be lost for registration remained very low (< 2%), even at 5 years after diagnosis.

Discussion

Our results showed overall high levels of completeness in Swiss cancer registration. An indirect measure of completeness is the DCN%. In Switzerland, high DCN% were found across all CRs only for hepatic (7.8%) and pancreatic (11.1%) cancer (Table 1). This is not unusual, but rather expected for cancers with a poor prognosis (Pollock and Vickers, 1995). DCN% must be higher than or equal to DCO%. The Swiss DCN% values are consistent with mean DCO% of 8.0 and 7.1% for hepatic and pancreatic cancer reported from 42 European CRs, respectively (diagnoses 2003–2007; Forman *et al.*, 2014). However, high DCN% alone is not a strong indicator for under-reporting, which is supported by the sparsity of flagging for hepatic and pancreatic cancer estimated by other methods in this study.

Another routinely used measure with implication for completeness is the proportion of diagnoses with microscopic verification, MV% (Table 1). Exceptionally high MV% might indicate over-reliance on the pathology laboratory as a source of information and failure to find cases diagnosed by other means (Bray and Parkin, 2009). BA was flagged for hepatic cancer with the unexpected high value of 94.4% compared with the value of 56.7% for Switzerland, which was similar to the mean of 47% from 56 CRs from European countries (Forman *et al.*, 2014).

The MI ratio is expected to be similar to 1–RS assessed in the same population at risk because both approximate cancer-specific case fatality (Parkin and Bray, 2009; Vostakolaei *et al.*, 2010). MI ratios systematically greater than their corresponding 1–RS values lead to a suspicion of under-registration. We consistently observed MI ratios significantly above the value of 1–RS for lymphoid leukaemia (Table 2). Also, the Flow method reported potential under-registration for lymphoid leukaemia in the majority of CR, with completeness levels of 67–88% at 3 years after diagnosis (Table 3). This result was not unexpected because 80% of lymphoid leukaemia diagnoses were of chronic types, compared with only 31% of all myeloid leukaemia diagnoses. Chronic types of leukaemia are often diagnosed in the outpatient setting, which potentially circumvents capture and registration compared with hospital-based diagnoses (Pritzkuleit *et al.*, 2008; Ess, 2009; Larsen *et al.*, 2009; Craig *et al.*, 2012; Dimitrova and Parkin, 2015). These haematological

malignancies come to the attention of CRs only after patients become hospitalized because the cancer progressed into a blast phase, causing long delays between diagnosis date and registration date. Such delays in registration of lymphoid leukaemia were apparent in Swiss CRs. Supplementary Table S3, Supplemental digital content 3, *http://links.lww.com/EJCP/A168* tabulates the time required to capture 90% of the finally registered diagnoses for different types of cancer. Overall, it took most CRs about 1 year to collect 90% of diagnoses, but it differed by diagnostic group. Although breast cancer diagnoses were captured rather quickly (0.6 years on average), diagnoses for lymphatic leukaemia took the longest (2.6 years on average).

We observed a pattern of significantly high ΔMI-Surv values in BA (hepatic, pancreatic, ovarian cancer and all sites combined). Together with the reported flags for high DCN%, significantly high MV% and significantly high MI ratios, it supports under-registration for at least some of the cancer sites involved.

The Flow method, but not the MI-Surv method, flagged prostate and kidney cancer and non-Hodgkin lymphoma as possibly under-registered at 3 years after diagnosis in ZH. ZH has in fact experienced reluctance in reporting of cases by some of the data sources because of unresolved issues of data protection legislation for the main part of the incidence period in this report (2007–2011) (Dehler *et al.*, 2012). This might have caused the longer registration delay of about 2 years on average, compared with 1 year in other CRs (Supplementary Table S3, Supplemental digital content 3, *http://links.lww.com/EJCP/A167*), as well as lower completeness estimates for all cancers combined at 1–3 years after diagnosis shown in Supplementary Table S2 (Supplemental digital content 2, *http://links.lww.com/EJCP/A167*). The issues with data protection legislation have been resolved recently (Dehler *et al.*, 2014).

Limitations

The methods used rested on a number of assumptions. The value of ΔMI-Surv will be affected not only by under-registration but also by inaccurate or incomplete registration of causes of death, or biased RS estimates. The quality of the Swiss vital statistics is high because only about 3% of all deaths have an unknown cause (Roy and Junker, 2014). We observed that 11% of all deaths between 2006 and 2011 were assigned to ill-defined codes as the principal cause (i.e. symptoms, signs, ill-defined conditions, deaths from injuries where the intent is not determined, cardiac arrest, heart failure, or cancer codes for secondary, unspecified or multiple sites), which places Swiss vital statistics in the high-quality to medium-quality range compared with other European countries (Mathers *et al.*, 2005). Also, metastases may have misled the doctor certifying the death about the location of the primary cancer. The bias of ill-defined or incorrect causes of death exerted on the MI-Surv method are underestimation of the MI ratio, thus potentially masking existing under-registration.

Excluding DCO cases from survival analysis may bias survival as being too high (Robinson *et al.*, 2007; Holleczek and Brenner, 2012). The highest DCO% were found in BA (17.1% for pancreatic cancer and 10.7% for hepatic cancer) because trace-back is not systematically performed. As ΔMI-Surv values in BA were large (>50%), it is not likely that biased survival alone is responsible. Breast and prostate cancer are candidates for being affected by lead-time and length-time biases and overdiagnosis because of screening. This would overestimate survival or underestimate the expected MI ratio, and reduce the ability of the MI-Surv method to discriminate against under-registration.

The Flow method assumes that patients are not registered from sources other than death certificates after death, that is cases who died before registration and whose death certificate lack a mention of cancer are lost to the registration process (Bullard *et al.*, 2000). The proportion of registrations after death without cancer mentioned in the death certificate to all registrations after death amounted to 8% in ZH, 1% in FR, 7% in TI, 12% in VS, 13% GE, 9% in SG and 11% in GG. The proportion lost from registration will thus be slightly overestimated. As lost proportions were generally small (Supplementary Table S2, Supplemental digital content 2, *http://links.lww.com/EJCP/A167*), this will not affect the completeness value to a great extent.

Conclusion

Despite the fact that cancer is not yet mandatorily reportable in Switzerland, neither the MI-Surv method nor the Flow method detected signs of potential underascertainment of cases for most types of cancer in any CR tested, with the notable exception of lymphoid leukaemia. As next steps, we will follow up flagged cancer types in individual CRs to substantiate these findings and identify ways of improvement, such as optimized matching of mortality to registration data. Future studies will include in-depth analyses of completeness depending on factors such as age at diagnosis or analyses of temporal completeness trends.

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Conflicts of interest

There are no conflicts of interest.

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